REMARKS

The Applicants request reconsideration of the present application in view of the foregoing amendments and the following remarks.

I. Amendments to the Specification

The Specification currently is amended to correct obvious errors. These obvious errors include typographical errors in some of the Examples where the units of irradiation should be expressed as power per unit area, for example "mW/cm^2" or "$mW \cdot cm^{-2}$", rather than "mW/cm^{-2}". One skilled in the art would recognize that irradiation for polymerization is expressed as power per unit area and that the reference to "mW/cm^{-2}" is an obvious error.

These obvious errors in the Specification also include references to an "E modulus" or "Young's modulus" where obviously the Specification should refer to a "shear modulus." In support of the Applicants' contention that these amendments correct obvious errors and do not introduce new matter, the Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 by Dr. Timothy Hughes, (hereinafter "Hughes Declaration I"). Dr. Hughes is a listed co-inventor for the application.

As indicated in the Hughes Declaration I, the obvious errors relate to the discussion in the Specification where the "E modulus" or "Young's modulus" is asserted to be measured by a rheometer such as a Micro Fourier Rheometer (MFR). One skilled in the art would recognize that this is an obvious error where an MFR is not used to measure the "E modulus" or "Young's modulus" of a polymer. Rather, an MFR is used to measure the "shear modulus" of a polymer. Furthermore, the original Specification contemplates measuring the shear modulus stating that

> One measure of the mechanical properties is the flexibility of such a polymer as measured by its elasticity modulus (as measured by its E modulus). The polymer ***shear modulus*** is a related property that may be measured also. Both can be measured as the force

> required to deform a product, such as a lens, formed by the polymer by measuring stress against strain. This ***E modulus*** of the polymer of the invention may be measured by a Micro Fourier Rheometer. A Bohlin controlled stress rheometer may also be used. For a lens application of this invention, the ***E modulus*** measured by a Micro Fourier Rheometer in this way is preferably in the range 0.01-100 kPa, preferably 0.1-10 kPa and most preferably 0.1-5 kPa.

(*See* Specification at page 10, lines 5-13 (emphasis added)). Clearly, this paragraph includes obvious errors where this paragraph refers to measuring the "E modulus" (*i.e.*, "Young's modulus") with an MFR. One skilled in the art would recognize that this paragraph should refer to measuring the "shear modulus" with an MFR. Likewise, Examples 2, 4, 6, 8, 10, 11, and 13 include obvious errors because these Examples refer to measuring "Young's modulus" (*i.e.*, the "E modulus") with an MFR. One skilled in the art would recognize that these Examples should refer to measuring the "shear modulus" with an MFR.

Therefore, the amendments to the Specification correct obvious errors and do not introduce new matter. Entry thereof is requested.

II. <u>Amendments to the Claims</u>

This amendment adds, changes and/or deletes claims in this application. A detailed listing is presented, with an appropriate defined status identifier, of all claims that are or were in the application, irrespective of whether the claim(s) remain under examination.

In order to advance prosecution, the Applicants have requested the cancellation of claim 27, without disclaimer or prejudice to further prosecution.

In order to advance prosecution, claims 5, 8, 11, 14, 15, 18, 19, 22, and 24 currently are amended. Claims 36-40 are requested to be added.

In particular, claim 5 is amended to recite "A biomedical implant comprising a polymer that is cured from a composition comprising a random or block macromonomer of general formula...." Claims 8, 11, 14, 15, 18, 19, 22, which depend from claim 5, similarly are amended to recite biomedical implants. Claim 32 depends from claim 5 and recites that the biomedical implant is an intraocular lens. New claims 36-39 depend from claim 5 and recite that the biomedical implant is a breast implant, a soft tissue replacement, a soft tissue filling agent, and a vitreous/aqueous humor replacement, respectively. These amendments are supported in the original specification where the application is drawn to biomedical compositions that may be cured in vivo to form implants. (*See, e.g.*, Specification at page 9, lines 19-27). The original Specification states that the disclosed macromonomers may be used as injectable precursors for forming biomedical implants, which may include intraocular lenses, breast implants, soft tissue replacements, soft tissue filling agents, and vitreous/aqueous humor replacement. (*See id.*)

Claim 5 also is amended to indicate that the claimed implant has a suitable elasticity. As amended, claim 5 recites that "the macromonomer is curable in vivo and when polymerized to form the cured polymer, the polymer has a shear modulus as measured by a Micro Fourier Rheometer between 0.1 and 5 kPa." Support for this amendment is provided in the Specification. (*See, e.g.*, Specification at page 9, lines 5-13).

New claim 40 depends from claim 5 and recites that "the composition has a viscosity of 1,000 – 60,000 cS at 25°C and the polymer comprises at least 80% of the macromonomer by weight." Support for new claim 40 is provided in the original Specification. (*See, e.g.*, Specification at page 10, lines 26-30; and at page 13, lines 2-4.)

Because the foregoing amendments do not introduce new matter and otherwise are proper, entry thereof is requested. After the claims are amended as set forth above, claims 5, 8, 11, 14, 15, 18, 19, 22, 24, 32, and 36-40 are pending in the application.

III. Claim Rejections – 35 U.S.C. § 102(e) over Lutz *et al.*

Claims 5, 8, 11, 15, 18, and 27 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Lutz *et al.*, (U.S. Patent No. 5,246,979) (hereinafter "Lutz"). The Office Action asserts that Lutz teaches acrylamide-functionalized polymers meeting all the limitations of the aforementioned claims at columns 3-5 and particularly, lines 12-30. The Applicants respectfully traverse the rejection in view of the foregoing amendments and for the following reasons.

As amended, claim 5 recites:

> "A biomedical implant comprising a polymer that is cured from a composition comprising a random or block macromonomer of general formula…";
> "the macromonomer contains at least one pendant Z"; and
> "the macromonomer is curable in vivo and when polymerized to form the cured polymer, the polymer has a shear modulus as measured by a Micro Fourier Rheometer between 0.1 and 5 kPa."

Lutz does not teach or suggest a biomedical implant meeting all of the limitations of claim 5. Therefore, Lutz does not anticipate the present claims. Although Lutz discloses general formulas for polydiorganosiloxanes at column 5, lines 12-30, Lutz does not teach or suggest a biomedical implant that comprises a polymer formed from the disclosed polydiorganosiloxanes and having the structural and functional properties recited in claim 5.

The Applicants have identified macromonomers that are suitable for curing in vivo to form polymers that may be utilized as biomedical implants. Accordingly, the polymers have a desirable elasticity. This aspect is recited in the present claims. Lutz does not teach or suggest macromonomers that are cured in vivo in order to prepare polymers for biomedical implants, let alone biomedical implants having the desired elasticity as recited in claim 5.

In order to achieve polymers having the recited structural and functional properties, claim 5 recites that the macromonomer "contains at least one pendant Z." In addition, the formula

recited in claim 5 also requires at least one terminal Z. These requirements relate to "cross-link density" of the claimed macromonomers and are important in order to ensure that each macromonomer is cross-linked in vivo and does not leach from the site of polymerization as an "extractable." Although Lutz states that "[t]he polyorganosiloxane has on the average at least 0.4 Z per molecule," (see column 5, lines 18-19), Lutz does not teach or suggest that it is required that each macromonomer include at least one pendant Z (and at least one terminal Z), as required in the present claims. In fact, for the lowest level of functionalization of Lutz's macromonomers, 3 out of every 5 macromonomers will not contain a cross-linkable group at all (on the basis that 0.4 = 2/5). In contrast, the macromonomers defined by the presently amended claims require at least one pendant Z and at least one terminal Z per macromonomer, based on the formula recited in claim 5.

In addition, after Applicants' macromonomers are polymerized to form a cured polymer, the polymer has a suitable elasticity, where the cured polyer "has a shear modulus as measured by a Micro Fourier Rheometer between 0.1 and 5 kPa." This limitation on the shear modulus correspondingly places a structural limitation on the cross-linking density of the macromonomer which is not taught or suggested by Lutz. This recited elasticity of the polymer is important in order for an implant comprising the polymer to mimic the biological tissue which it replaces. For example, where the polymer is utilized as part of an intraocular lens, the recited flexibility for the polymer is important in order for the implant to be manipulated by the ciliary muscles. (*See* Specification at page 8, lines 1-4).

In summary, Lutz does not teach or suggest a biomedical implant, let alone a biomedical implant comprising a polymer with the structural and functional properties recited in claim 5. Therefore, claim 5 and those claims that depend from claim 5 are patentable over Lutz.

For all these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(e) over Lutz are requested.

IV. Claim Rejections – 35 U.S.C. § 103(a) over Hodd *et al.*

Claims 5, 8, 11, 18, 19, 22, 24, 27, and 32 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hodd *et. al.* (U.S. Patent No. 6,737,496) (hereinafter "Hodd"). The Applicants respectfully traverse the rejection in view of the foregoing amendments and for the following reasons.

First, the Applicants submit herewith a Declaration under 37 C.F.R. § 1.132 by Dr. Timothy Hughes related to the non-obviousness of the presently claimed subject matter (hereinafter "Hughes Declaration II"). The Applicants submit that the claimed subject matter is non-obvious for reasons discussed in the Hughes Declaration II and furthermore for the following reasons.

A. Hodd Does Not Enable One Skilled in the Art to Make the Biomedical Implants of the Present Claims

The Office Action tacitly acknowledges that Hodd does not disclose a macromonomer meeting all the limitations of the claims where the rejection is for "obviousness" and not for "anticipation." The Office will appreciate the fact that even for a rejection based on "obviousness" the cited reference must enable one to make and use the subject matter of the rejected claim. The Applicants respectfully submit that Hodd does not enable one skilled in the art to make and use the subject matter of the rejected claims.

Claim 5 recites that "the macromonomer is curable in vivo and when polymerized to form a cured polymer, the polymer has a shear modulus as measured by a Micro Fourier Rheometer between 0.1 and 5 kPa." As indicated in the Hughes Declaration II, the recited polymer will have an elasticity that is comparable to that for a natural lens. Although Hodd appreciates the desirability of forming polymers having an elasticity that is comparable to that for a natural lens, Hodd does not teach how to make such polymers.

In the Background of the Invention, Hodd states that "to respond to the accommodating forces of the eye, the compression modulus of IOL should be comparable to that of the natural lens which is in the range of about 1 to 5 kPa." (*See* Hodd, col. 1, lines 39-42). Hodd's statement relates to the "compression modulus." As indicated in the Hughes Declaration II, the compression modulus and shear modulus are related moduli for reporting elasticity. (*See also* "Modulus of Elasticity" from INSTRON Corporation, enclosed herewith, discussing the compressive modulus of elasticity and the shear modulus of elasticity). The Applicants submit that where Hodd refers to the "compression modulus," Hodd actually should refer to the "shear modulus." Furthermore, the Applicants contend that the elasticity of an intraocular lens (IOL) should be about 0.1 to 5 kPa when measured as a shear modulus using a rheometer such an MFR. However, Hodd does not teach how to make an intraocular lens having a shear modulus between about 0.1 to 5 kPa or an intraocular lens having a compression modulus between about 0.1 to 5 kPa for that matter.

Although Hodd initially discusses the desirability of a polymer having a compression modulus in the range of about 1 to 5 kPa, Hodd later states in the Description of the Invention:

> "Further, by employing the polysiloxanes with functional acryl groups, the injectable material and the methods of the present invention lenses with a compression modulus suitable to undergo accommodation by the forces of the eye can be obtained. Typically, lenses having a modulus below about 55 kPa and ***in the range of about 20 to 50 kPa*** can readily be obtained by employing the present invention which are functionally accommodatable by the human eye."

(*See* Hodd, col. 6, lines 37-44, (emphasis added)). Therefore, Hodd indicates that the disclosed polymers have a compression modulus in the range of about 20 to 50 kPa. The Applicants respectfully disagree that a polymer with a compression modulus of about 20 to 50 kPa has the most suitable elasticity for use as an IOL. However, Hodd's statement suggests that the disclosed macromonomers cannot be utilized to form polymers having a compression modulus

below 20 kPa or, as discussed in the Hughes Declaration II, a shear modulus between about 0.1 to 5 kPa.

Although Hodd's initial discussion regarding elasticity relates to the compression modulus, Hodd later measured the shear modulus of the disclosed polymers in the Examples. In the Table at column 11, Hodd discloses the rheological measurements of photocured materials. Hodd prepared polymers in Example 9 and then assessed the elasticity of the prepared polymers by measuring the shear modulus with a Rheometrics RDA 2 rheometer, which will provide a comparable measure of shear modulus as the Micro Fourier Rheometer (MFR) used in the present application. (*See* Phan-Thien *et al.*, RHEOL ACTA 35:410-416 (1996) (enclosed herewith)).

As indicated in Hodd at the Table at column 11, none of the prepared polymers had a shear modulus less than 21 kPa and some had a shear modulus as high as 65.3 kPa. This range of 21 to 65.3 kPa for the measured shear modulus corresponds roughly to the range of 20 to 50 kPa discussed initially in Hodd where Hodd states "[t]ypically, lenses having a modulus below about 55 kDa and in the range of about 20 to 50 kPa can readily be obtained by employing the present invention which are functionally accommodatable by the human eye." (*See* Hodd, col. 6, lines 37-44). Regardless, Hodd clearly does not teach how to make a polymer having a shear modulus between 0.1 to 5 kPa using the disclosed macromonomers. In contrast, the Examples of the present application teach how to make a polymer having a shear modulus between 0.1 and 5 kPa using the disclosed macromonomers.

B. Applicants Discovered a Non-obvious Solution to an Unsolved Problem

As previously discussed, the macromonomers of the present invention are utilized to prepare polymers for biomedical implants. The claimed macromonomers provide decreased

extractables, sufficiently low modulus, and sufficient viscosity for injectability for in vivo curing. These aspects are encompassed in the claimed subject matter.

The macromonomers of the present invention must have at least one pendant and at least one terminal Z group with the advantages of these features being described in the Specification. (*See* Specification, page 7, line 15, to page 8, line 16). In particular, higher molecular weight macromonomers with more cross-linkable groups per chain (assuming cross-link density remains constant) contain a decreased amount of extractables. (*See* Specification, page 7, line 26 to page 8, line 1). However, a higher molecular weight also causes a higher viscosity and therefore a decrease in the ease of injectability for curing in vivo. (*See* specification, page 8, lines 9-11). The present inventors have found that using a combination of both pendant and terminal cross-linkable groups results in a better ability to balance these competing considerations (*See* Specification, page 8, lines 14-16).

The presently claimed subject matter is patentable over Hodd because the use of both terminal and pendant functional groups is not an obvious solution to this unsolved problem in the art. Hodd teaches polymers having a shear modulus of no less than 21 kDa. One seemingly obvious way to reduce the modulus to the range recited in claim 5 is to reduce functionalization, for example, by:

a) not functionalizing some percentage of the total macromonomers (which may then result in some macromonomers leaching out – an unacceptable outcome for curing in vivo);
b) including a plasticizer in the macromonomer composition (which may also leach out – another unacceptable outcome); or
c) increasing the average molecular weight of the macromonomer per functional group in order to "dilute" the functionalization (but this may unacceptably increase the viscosity of the uncured composition and hinder injection prior to curing in vivo).

The present inventors surprisingly have discovered that a combination of terminal and pendant functionalization achieves the requirements of claim 5 without these unacceptable side effects.

Clearly, utilizing macromonomers that have both terminal functional groups and pendant functional group was not an obvious solution to this unsolved problem in the art. These issues are discussed further in the Hughes Declaration II at numbers 16-22.

All of the Examples in Hodd relate to macromonomers having terminal functional groups. The only instance where Hodd might reasonably be considered to contemplate macromonomers having both pendant and terminal functional groups is at column 3, line 64 to column 4, line 1, where Hodd states:

> Functional acryl groups are defined herein by that at the polysiloxane molecules have functional groups attached thereto including an acryl group moiety, so as to become acryl-bearing, by acryl attachment to the siloxane monomers of the polysiloxane backbone, its terminal ends, or both.

Based on this statement, Hodd might suggest the possible use of: (1) macromonomers with pendant functional groups; (2) macromonomers with terminal functional groups; or (3) macromonomers with pendant functional groups and terminal functional groups. However, of these possibilities, there is no suggestion in Hodd to utilize specifically macromonomers with both pendant functional groups and terminal functional groups to prepare polymers having a shear modulus between 0.1 to 5 kPa.

In fact, based on Hodd's teachings one skilled in the art might be dissuaded from using a macromonomer having both pendant functional groups and terminal functional groups to prepare polymers having a shear modulus between 0.1 to 5 kPa. All of the Examples in Hodd relate to macromonomers with terminal functional groups and all of the prepared polymers in the Examples had a shear modulus greater than 21 kPa. If one skilled in the art were to add pendant functional groups to the macromonomers disclosed in Hodd's Examples, the resultant macromonomers having both terminal functional groups and pendant functional groups would be expected to crosslink even more efficiently. Therefore, the resultant macromonomers having

both terminal functional groups and pendant functional groups would be expected to produce polymers having a shear modulus even higher than 21 kPa. Accordingly, Hodd provides no motivation to create and utilize macromonomers with both terminal functional groups and pendant functional groups in order to prepare polymers having a shear modulus between 0.1 to 5 kPa.

For all these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) over Hodd are requested.

V. **Conclusion**

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is requested to contact the Applicants' representative if a telephone interview will advance prosecution.

Respectfully submitted,

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